Morphological Diversity of DNA-Colloidal Self-Assembly

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We study theoretically a binary system in which an attraction of unlike particles is combined with a type-independent soft-core repulsion. The possible experimental implementation of the system is a mixture of DNA-covered colloids, in which both the repulsion and the attraction may be induced by DNA solution. The system is shown to exhibit surprisingly diverse and unusual morphologies. Among them are the diamond lattice and the membrane phase with in-plane square order, a striking example of *spontaneous compactification*.

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Colloidal self-assembly has attracted a lot of interest across several disciplines. It is widely used as a model system for study of crystallization and glassiness [1]. It also has a great technological potential, e.g., as a fabrication technique for photonic band gap materials [2]. A monodisperse colloidal system would typically crystallize into a closed-packed structure or body-centered cubic (bcc) lattice [1,3]. In this Letter, we propose a system which combines relatively simple interactions with considerably more diverse and unexpected phase behavior.

Our study is inspired by a recent experimental demonstration of DNA-assisted self-assembly of nanoparticles [4,5]. The key elements of that scheme are submicron spheres covered with short single-stranded DNA "markers." The marker sequence determines the particle type (there may be many markers per particle, but their sequences must be the same). One can now introduce type-dependent interactions between the particles by adding "linker" DNA molecules, whose ends are complementary to the corresponding markers. These interactions are very selective, reversible, and tunable.

In the first part of this Letter, we discuss a generic model in which the physical origin and details of the interparticle interactions are largely ignored. Let us consider a binary system of hard spheres, of the same diameter d, in which the particles belonging to different types (A and B) may create a reversible contact with binding energy $-E$. On the other hand, let same-type particles repell each other with a soft-core potential, $U(r)$. We study the phase behavior of the system for various values of two parameters: the aspect ratio, d/ξ [ξ is the range of potential $U(r)$], and the relative strength of the attraction, E/U_0 [here $U_0 \equiv U(d)$]. Later in the Letter, we discuss how this system can be implemented experimentally. Our specific proposal is to use DNA to introduce type-dependent attraction, and polymeric brush (possibly, also made of DNA) to induce the repulsive potential.

The nontrivial phase behavior of the discussed system is a result of interplay between the adhesive energy and the soft-core repulsion. We consider only structures with a 1 : 1 composition. Let r_k be a distance to the kth nearest neighbor of a particle in a given structure ($r_1 \equiv d$), let Z_k be the average number of such neighbors, and let Z be the average number of cohesive contacts per particle (coordination number). If the entropic effects are neglected, the energy per particle (i.e., the average chemical potential of A and B particles) is given by

$$\mu = \frac{1}{2}\left(-ZE + \sum_{k=2}^{\infty} Z_k U(r_k)\right) \simeq \frac{1}{2}[-ZE + Z_2 U(r_2)]. \quad (1)$$

Here, we have neglected the contribution from the interactions with the particles beyond the second nearest neighbors, which is a reasonable approximation for $d/\xi \gg 1$. In order to assure its validity, we have performed an *a posteriori* check of the effect of the higher-order corrections on our results. It is straightforward to use the above equation to identify the phase boundary between two different structures. Since the chemical potential should be continuous at the transition, one can express the critical value of adhesive energy E in terms of the geometrical parameters (Z, Z_2, and r_2) of the two phases

$$E \simeq \frac{Z_2' U(r_2') - Z_2 U(r_2)}{Z' - Z}. \quad (2)$$

The task of identifying all plausible morphologies of our system is clearly more challenging than comparing them energetically. There is hardly any systematic way of doing this. Nevertheless, one can considerably limit the search by making a number of assumptions based on general principles [6]: (i) In order to avoid the direct contacts between the same-type particles, the structures should be bipartal; i.e., they should consist of two sublattices corresponding to the two types of particles, so that all the nearest neighbors were of the opposite types; (ii) all the nearest neighbors should have the same bond length; This is needed to take advantage of the cohesive energy, as long as we model the particles as rigid sticky spheres; (iii) since the equilibrium structure is likely to possess a high symmetry, we consider only crystalline morphologies, in which all the sites are equivalent.

Note that in the limit of a large aspect ratio, among various phases with the same coordination number Z, the one with the largest r_2 is energetically preferred, independently on the number of the second nearest neighbors (Z_2). Since r_2 typically decreases with Z, the transition value of E, given by Eq. (2), asymptotically reaches the value $Z_2 U(r_2)$, determined by the parameters (Z_2, r_2) of the higher Z phase. One can conclude that the sequence of the phases in the large aspect ratio regime is generic and should be independent of the particular choice of the repulsive potential: bcc ($Z = 8$); simple cubic (sc, $Z = 6$); honeycomb stacking (HS, $Z = 5$); diamond (D, $Z = 4$). The prediction of a self-assembled diamond lattice is especially exciting, because of its potential as a photonic bad gap structure [2]. No true phase transitions are expected for $Z < 3$ because of the low dimensionality of the dominant structures.

As the aspect ratio D/ξ is being decreased, other equilibrium phases may appear. Figure 1(a) shows the phase diagram obtained for the exponential potential, $U(r) = U_0 \exp[-(r - d)/\xi]$. One feature which is particularly striking is that at a certain aspect ratio, the system undergoes a transition from 3D diamond lattice to quasi-2D membrane with in-plane square order (SQ). Even though this order is known to be strongly affected by long-range fluctuations [3], these fluctuations do not give any divergent contributions to the chemical potential of the 2D phase. Moreover, the entropy gain due to relatively strong out-of-plane fluctuations makes the SQ phase more favorable than an alternative 3D structure with a locally identical single-particle neighborhood [which can be constructed by starting with a cubic lattice and removing all the sites with indices $(2n, 2m, 2k)$ and $(2n + 1, 2m + 1, 2k + 1)$] [7]. The D-SQ transition which involves a change in effective dimensionality of the structure may be called *spontaneous compactification*. It is remarkable that, unlike similarly looking lipid membranes, the predicted quasi-2D phase is built by particles with isotropic effective interactions. Similarly, the diamond phase in our system is a result of the interplay of relatively simple *isotropic* potentials, in striking contrast with diamond morphologies found in nature. Recent studies indicate that the diamond phase can also be self-assembled from star polymers [8]. It is possible that the underlying physics in the two cases is similar.

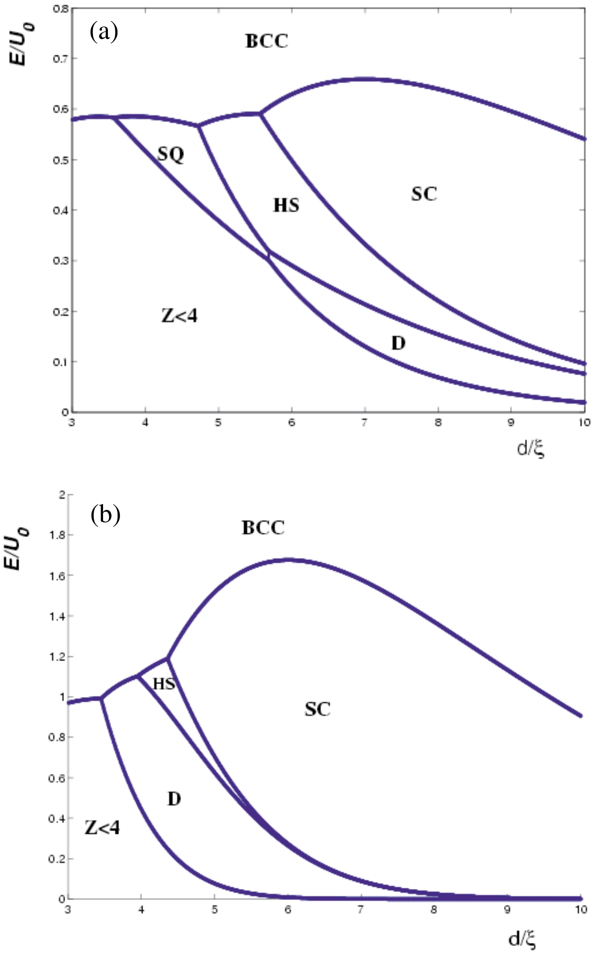

FIG. 1 (color online). Calculated phase diagram of the system for exponential (a) and Gaussian (b) forms of the repulsive potential $U(r)$.

As we have argued, the major features of the obtained phase diagram should be quite independent of the choice of the repulsive potential. To check this, we have studied the phase behavior for two types of soft-core repulsion, exponential and Gaussian, $U(r) = \exp[-(r - d)^2/2\xi^2]$ (see Fig. 1). The major difference is that the square lattice (SQ) completely disappears in the Gaussian case. On the other hand, the diamond lattice (D) significantly expands at the expense of the SQ and HS phases. This trend appears to be generic: the balance between the two competing $Z = 4$ phases, D and SQ, shifts towards diamond for potentials with a superexponential decay, while the region of stability of SQ expands for subexponential $U(r)$ (such as power laws, stretched exponential, or Yukawa interaction).

It should be pointed out that the above results cannot be interpreted as a perturbation of a well-studied phase diagram of the purely repulsive system. In that case the phase transitions are dominated by entropic effects. The behavior of the repulsive system is essentially lyotropic, i.e., the principle control parameter is osmotic pressure (or average density), and the crystallization is impossible without compression. In our case, the thermal corrections were neglected, and the osmotic pressure was assumed to be virtually zero. More precisely, the predicted crystals would coexist with the gaseous phase of an exponentially low volume fraction, $\Phi \sim \exp(\mu/kT)$. As long as the applied osmotic pressure remains well below kT/d^3, it is not expected to make any effect on the phase diagram. Note that within our original model, all the crystalline phases have zero compressibility. Since the particles were modeled as rigid spheres, the bond length had to be exactly equal to the diameter d. It is, however, quite easy to generalize this model by assuming a finite bond rigidity, κ. This is equivalent to the (morphology-dependent) renormalization of the repulsive potential: $\tilde{U}(r) = U(r) - Z_2(dU/dr)^2/2\kappa Z$, and the phase behavior does not change qualitatively as a result of this modification [7]. Similarly one can check that the results are robust with respect to the introduction of modest thermal fluctuations.

We now proceed with the discussion of a plausible experimental implementation of the proposed system. As we have already mentioned, type-dependent "DNA bridging" of colloidal particles is an appealing way to introduce the AB attraction. As to the soft repulsive potential, here we focus on a particular scenario in which this interaction is also induced by DNA. Namely, in addition to linker molecules we introduce DNA with only one "sticky end" (complementary to either A or B markers). These one-arm molecules do not result in bridging and play the role of a buffer (see Fig. 2). We will assume that both the buffer DNA and the linkers are double stranded, with the exception of the short terminal segments. The strength of the interaction of these sticky ends with the complementary markers can be characterized by DNA concentration c_0, at which the condensation would occur (i.e., when the chemical potential of an adsorbed chain would become equal to that in the solution). If the actual concentration of the buffer DNA, c, is much lower than c_0, the number of the adsorbed chains per particle is $N = N_{\max} c/c^{(0)}$. Here $N_{\max}$ is the total number of markers per particle. For the sake of simplicity, we assume that $N^{\max}$ and N are the same for A and B particles, i.e., $c_A/c_B = c_A^{(0)}/c_B^{(0)}$. It is very important that both linker and buffer-DNA molecules adsorb to the particles *reversibly,* so that the experimental time is long enough for our subsystem to reach an equilibrium with DNA solution.

A double-stranded DNA molecule can be described as a Gaussian chain, as long as its length L exceeds the persistence length, $l_p \simeq 50$ nm, and the probability of self-crossing, $sL^{1/2}/l_p^{3/2}$, remains small ($s \sim 1$ nm is an effective cross section). In other words, the excluded volume effects are negligible for $L \ll l_p^3/s^2 \sim 10^3 l_p$. Thus, the adsorbed DNA molecules can be treated as phantom Gaussian chains, which interact only with hard surfaces of the particles, but not with each other. Since the adsorption is reversible, the confined chains are being "squeezed out" when the gap between two particles, $r - d_0$, becomes comparable to the gyration radius of the DNA chain, R_g. A detailed discussion of the energetic penalty associated with this depletion can be found in Ref. [9]. As is shown there, the corresponding repulsive potential can be calculated in the spirit of Deryagin approximation, [10] (from now on, we distinguish bare particle diameter, d_0, and bond length d):

$$U(r) \simeq 2NkT\frac{R_g}{d_0}\int_{(r-d_0)/R_g}^{\infty}\left[1 - \exp\left(-\frac{W(\Delta)}{kT}\right)\right]d\Delta. \quad (3)$$

Here $W(\Delta)$ is the free energy penalty for the confinement of a Gaussian polymeric chain between two walls at separation $R_g\Delta$. It can be obtained by using the Schrödinger-like description of the ideal polymer [11,12]:

$$\frac{W(\Delta)}{kT} = \log\left\{\frac{\sqrt{2/3}}{\Delta}\sum_{n=0}^{\infty}\exp\left[-\frac{1}{6}\left(\frac{\pi(1+2n)}{\Delta}\right)^2\right]\right\}. \quad (4)$$

The resulting repulsive potential is shown in Fig. 3.

The attractive potential induced by the linker DNA can be calculated in a very similar manner. Important differences are that one has to take into account the elastic energy of a stretched linker, $W_{\mathrm{el}}(\Delta) = 3kT\Delta^2/2$, and that the condensation concentration of the chains with two

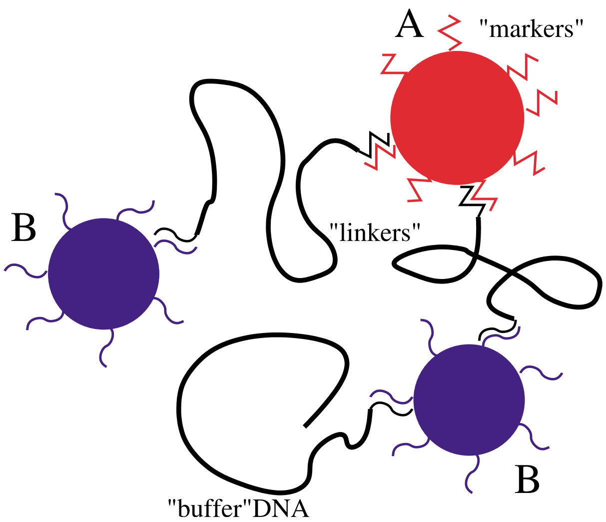

FIG. 2 (color online). Suggested experimental scheme.

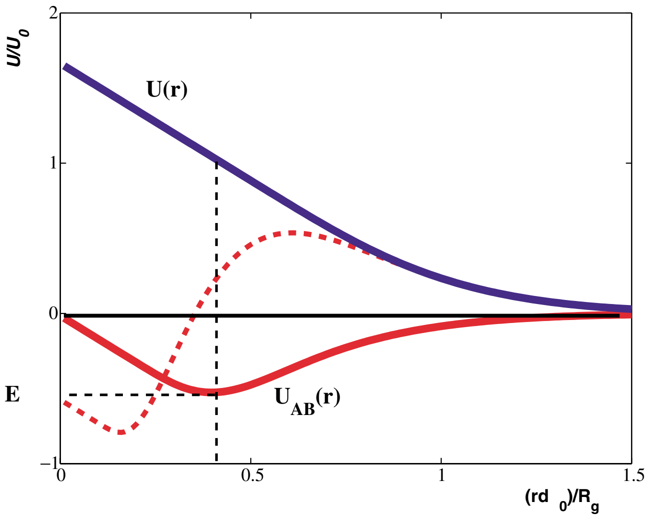

FIG. 3 (color online). Repulsive, $U(r)$, and attractive, $U_{AB}(r)$, potentials induced by DNA-particle interactions. The solid lines correspond to $R_g'/R_g = 1$. Note the barrier in the attractive potential for $R_g'/R_g = 0.5$ (dashed line).

sticky ends is given by $c_{AB}^{(0)} = c_A^{(0)} c_B^{(0)} R_g'^3$. Note that in a general case the gyration radius of a linker DNA, R_g', may be different from R_g.

$$U_{AB}(r) \simeq U(r) - \frac{2N_{\max}^2 kT}{3} \frac{c_{AB}}{c_{AB}^{(0)}} \left(\frac{R_g}{d_0}\right)^3 \times \int_{(r-d_0)/R_g}^{\infty} \exp\left[-\frac{W(\Delta) + W_{\mathrm{el}}(\Delta)}{kT}\right] d\Delta. \tag{5}$$

As one might expect, the tail of repulsive potential $U(r)$ is well described by a Gaussian with the characteristic length scale $\xi \simeq R_g$:

$$U(r) \sim \exp\left[-\frac{3}{2}\left(\frac{r-d}{R_g} + \beta\right)^2\right]. \tag{6}$$

Here d is the effective diameter which is determined by the position of the minimum of $U_{AB}(r)$, and the bias $\beta \simeq 0.15 + (d - d_0)/R_g$. For the case $R_g'/R_g = 1$, shown in Fig. 3, $\beta \simeq 0.6$. Thus, the corresponding phase diagram should be somewhere halfway between the Gaussian and exponential ones. By increasing the ratio R_g'/R_g one can move the system more towards the exponential regime, because the position of the minimum changes roughly linearly with the radius of the linker DNA. However, the dynamic range of R_g'/R_g is rather limited: the long linkers would result in the additional attraction beyond the nearest neighbors, which would violate our initial assumptions. At the opposite regime, $R_g' < R_g$, the particles need to overcome a significant energetic barrier before they start feeling the attraction (see Fig. 3). The existence of this barrier is the major reason why we suggest to use linkers of at least several persistence lengths (i.e., about 1 kBase for dsDNA). In this case, the Gaussian description is applicable. As we have shown, when the gyration radius of the linkers matches the scale of the repulsive potential, the particles may create a bound state without the need of overcoming any barrier. If the linkers are made of double-stranded DNA, the optimal length scales are $\xi \sim l_p \sim 0.1$ μm and $d \sim 1$ μm

According to Eqs. (3)–(5), the relative strength of the attraction and the repulsion is controlled by the ratio of the concentrations of the linkers and buffer DNA:

$$\frac{E}{U_0} = \frac{c_{AB}}{\tilde{c}_{AB}} - 1. \tag{7}$$

Here $\tilde{c}_{AB}$ is the linker concentration at which E vanishes. This concentration can be determined experimentally by observing the process of dimer binding/unbinding. If $R_g' = R_g$, $\tilde{c}_{AB} \simeq c_A c_B R_g^6/d^3$. Thus, by changing the ratio $c_{AB}/c_A c_B$, one can tune the control parameter E/U_0.

The fundamental time scale of the problem is determined by the lifetime of the AB bond,

$$\tau_0 \simeq \frac{\eta d R_g'^2}{kT} \exp\left(\frac{E}{kT}\right) \sim 10 \text{ s}. \tag{8}$$

Here η is the solvent viscosity, and the trial frequency is assumed to be limited by the particle diffusion rather than by the desorption rate of a linker DNA. At physiological conditions, this requirement limits the marker sequence to approximately ten bases. Note that at the optimal regime the characteristic energy scale $U_0 \sim E$ should be comparable to kT. The true relaxation time of the system is determined by slow aggregation and growth processes, and it might be much longer than τ_0. However, the crystal growth may be substantially accelerated by epitaxial nucleation near commensurate substrate [13], or by certain annealing procedures.

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